AMENDMENTS TO THE CLAIMS

1-4. (Cancelled)

5. (Currently amended) A method of screening a substance efficacious for healing, preventing or treating a vascular disorder resulting from abnormal uric acid uptake into a vascular smooth muscle cell or abnormal uric acid elimination by URAT1 in[[to]] a vascular smooth muscle cell, wherein the method comprises:

a. contacting a vascular smooth muscle cell with a test compound and urate;

b. measuring the amount ~~level~~ of uric acid ~~uptake or elimination~~ in i) the vascular smooth muscle cell, or ii) a medium comprising the vascular smooth muscle cell; ~~and~~

c. comparing the amount of uric acid with a control, wherein the control is i) the level of uric acid in a control vascular smooth muscle cell, or ii) the level of uric acid in a medium comprising the control vascular smooth muscle cell, respectively; ~~identifying the compound as a substance efficacious for healing, preventing or treating the vascular disorder~~ when ~~addition of the test compound reduces the level of uric acid uptake or increases the level of uric acid elimination in the cell~~

d. identifying the test compound as efficacious for healing, preventing or treating a vascular disorder when addition of the test compound increases or decreases the amount of uric acid in the vascular smooth muscle cell or in the medium comprising the vascular smooth muscle cell, as compared with the control.

6. (Previously presented) The method according to claim 5, wherein the cell is an umbilical vein epithelial cell.

7.-14. (Cancelled)

15. (New) The method of claim 5, wherein the method further comprises identifying the test compound as a uric acid uptake inhibiting substance when i) the amount of uric acid in the vascular smooth muscle cell is increased as compared to the

control, or ii) the amount of uric acid in the medium comprising the vascular smooth muscle cell is decreased as compared to the control.

16. (New) The method of claim 5, wherein the method further comprises identifying the test compound as a uric acid uptake promoting substance when i) the amount of uric acid in the vascular smooth muscle cell is decreased as compared to the control, or ii) the amount of uric acid in the medium comprising the vascular smooth muscle cell is increased as compared to the control.

REMARKS

Status of Claims and Support for Amendments

Claims 1-4 and 7 were previously cancelled and claims 8-14 are newly cancelled without prejudice or disclaimer. Claim 5 is amended, and new claims 15 and 16 are added.

No new matter is introduced by virtue of the within amendments; support therefor can be found throughout the specification and original claims.

Priority

The Office Action acknowledges receipt of the verified English translation of JP 2003-384863, as filed with the Japanese Patent Office on November 14, 2003. The Office Action indicates that the effective filing date of the present application is November 11, 2004, the date on which the priority international application (PCT/JP2004/016761) was filed. That said, it is well established and indicated in the MPEP at 706.02(b), that the foreign priority document may be used to overcome certain references.

Accordingly, it is respectfully submitted that Applicants' can rely on the Japanese priority date of November 4, 2003, to overcome references cited with a date subsequent.

Claims Rejections under 35 USC §112, 2nd paragraph

Claims 5, 6 and 8-14 are rejected under 35 USC §112, 2nd paragraph, as allegedly being indefinite. The Office Action asserts that "it is not clear, in the independent claims 5, 8, 10 and 14, how the uric uptake into the cell can be at the same time elimination of the uric acid into the cell".

Additionally, claims 5, 6 and 8-14 are rejected as being allegedly incomplete for omitting essential steps. The Office Action asserts at page 3, "The omitted steps are: performing the method on either a control cell or with a control substance and comparing the results in order to be able to identify the compound as useful."

As an initial matter, claims 8-14 have been cancelled, thereby rendering the rejections moot with respect to these claims. The cancellations were made solely to advance prosecution, and not in acquiescence to the rejections.

Applicants have amended the claims to clarify the features of the invention and address the noted informalities. As amended, each of the pending claims involves comparing the amount of uric acid in a test sample with the uric acid level found in a control sample. In addition, each of the pending claims distinguish between uric acid levels present in a vascular smooth muscle cell and uric acid levels in a medium containing a vascular smooth muscle cell. Transport of uric acid via URAT1 occurs through the cellular membrane and involves an exchange of uric acid and an anionic substance. Specifically, when an extracellular uric acid is taken up inside a cell, an intercellular anionic substance is eliminated outside the cell. Conversely, when an intercellular uric acid is eliminated outside the cell, an extracellular anionic substance is taken up inside the cell. Distinguishing between uric acid levels present in a vascular smooth muscle cell and uric acid levels in a medium containing a vascular smooth muscle cell is more descriptive of the mechanism of URAT1 uric acid transport.

In view of the foregoing, reconsideration and withdrawal of the rejection under 35 USC §112, 2nd paragraph, are requested.

Rejection under 35 USC §103(a)

Claims 5, 8-12, and 14 are rejected under 35 USC §103(a) over Endou et al. (CA 2456172, published April 3, 2003) ("Endou") in view of Kanellis et al. (*Hypertension*: 41, 1287-1293, 2003) ("Kanellis") and Hurteau et al. (*Cancer*, 74, 93-99, 1994) ("Hurteau").

The rejection is respectfully traversed. As indicated above, claims 8-12 and 14 have been cancelled, thereby rendering the rejection moot with respect to these claims. Additionally, claim 5 has been amended to further define the features of the invention and advance prosecution.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki,* 745 F.2d 1468, 1471-73 (Fed. Cir. 1984). As set forth in *Graham v. John Deere Co. of Kansas City*, "[u]nder § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined." 383 U.S. 1, 17 (1966). This has been the standard for over 40 years, and remains the law today. *See KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1734 (2007). If, after these criteria are considered, the evidence indicates that the claimed invention is obvious over the prior art, it may be said that a *prima facie* case of obviousness has been established.

Applicants respectfully assert that the Examiner has not met the burden of establishing a *prima facie* case of obviousness because one of ordinary skill in the art would not have arrived at the claimed invention based on the teachings of the cited references. The present claims are directed to a method of screening a substance efficacious for healing, preventing or treating a vascular disorder resulting from abnormal uric acid uptake into a vascular smooth muscle cell or abnormal uric acid elimination by URAT1 in a vascular smooth muscle cell. The method comprises, *inter alia*, contacting a vascular smooth muscle cell with a test compound and urate, and measuring the amount of uric acid in i) the vascular smooth muscle cell, or ii) a medium

comprising the vascular smooth muscle cell. In contrast, the Examiner characterizes Endou as disclosing "a novel urate transporter gene participating in the urate transport in the kidney and a urate transporter which is a polypeptide encoded by the above gene." Office Action, page 5 (emphasis added). A kidney cell, however, is not a vascular smooth muscle cell. Indeed, the Examiner admits that Endou "do[es] not mention specifically vascular smooth muscle cells." *Id.* at page 6. Thus, for at least these reason, Endou does not teach contacting a vascular smooth muscle cell with a test compound and urate, and measuring the amount of uric acid in i) the vascular smooth muscle cell, or ii) a medium comprising the vascular smooth muscle cell, as required in the present invention.

Kanellis and Hurteau do not cure the deficiencies of Endou. The Examiner characterizes Kanellis as allegedly teaching that "soluble uric acid can induce vascular smooth muscle cells proliferation [sic], activated through ERK, MAPK[,] Cox-2 or PDGF pathways [and] . . . that uric acid increases the production of MCP-1 protein in rat VSMC." Office Action, pages 6 and 7. Hurteau allegedly "exemplif[ies] a well-known and routinely [sic] use of thymidine incorporation assay for determining cell proliferation." *Id.* at page 7. Neither reference teaches contacting a vascular smooth muscle cell with a test compound and urate, and measuring the amount of uric acid in i) the vascular smooth muscle cell, or ii) a medium comprising the vascular smooth muscle cell, as required in the present invention.

The present invention is based on Applicants' discovery that URAT1 is expressed in vascular smooth muscle cells. With this knowledge, Applicants were able to invent a screening system that reflects the real conditions under which uric acid uptake and elimination occurs in the blood vessels of the heart. The present invention makes possible identifying agents that will be useful in treating vascular disorders resulting from abnormal uric acid uptake or elimination.

None of the cited reference teach that URAT1 is present on the surface of vascular smooth muscle cells. Without this key insight, one of ordinary skill in the art would not have been motivated to modify the disclosures in the cited references to

arrive at the claimed invention. Absent the teachings of the present application and without motivation to modify the disclosures in the cited references, a person of ordinary skill in the art would need to possess some level of prescience to arrive at the present invention. Although a person of ordinary skill in the art possesses "ordinary creativity" (KSR, 127 S.Ct. at 1742), the standard of obviousness under *KSR* does not require a person of ordinary skill in the art to possess any level of prescience.

Accordingly, for at least the above reasons, Applicants submit that the Examiner has not established a *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection are respectfully requested.

Double Patenting Rejection

Claim 5 is rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of USP 7,510,847 ("the '847 patent") in view of Kanellis. The Examiner asserts that "it would have been obvious to performed [sic] the method claimed in the '847 patent on [v]ascular smooth muscle cells as taught by Kanellis et al. with a reasonable expectation of success, because the assays were routinely used in the art and Kanellis et al. showed the usefulness of employing VSMC in finding modulators in uric acid pathogenesis" (Office Action, page 10).

Applicants respectfully disagree and traverse this rejection. Applicants respectfully assert that the claims of the '847 patent fail to render obvious the presently claimed invention.

As noted in MPEP § 804(III), "a double patenting rejection must rely on a comparison with the claims in an issued or to be issued patent, whereas an anticipation or obviousness rejection based on the same patent under 35 U.S.C. 102(e)/ 103(a) relies on a comparison with what is disclosed (whether or not claimed) in the same issued or to be issued patent." (emphasis added; formatting removed). Furthermore, inventions based on the identification or selection of a specific material or compound with particularly desirable properties within a previously claimed genus of such materials or compounds are patentably distinct from the prior claimed subject matter.

See e.g., *In re Kaplan*, 789 F.2d 1574, 1578, 1580 (Fed. Cir. 1986) (prior generic patent claim did not invalidate claim to later selected species for double patenting); *see also In re Ruschig*, 343 F.2d 965, 974-75 (C.C.P.A. 1965) (prior generic disclosure did not anticipate later selected species under 35 U.S.C. § 102); *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1340 (Fed. Cir. 2003) ("Improvement and selection inventions are ubiquitous in patent law . . ."); *In re Baird*, 16 F.3d 380, 383 (Fed. Cir. 1994) (prior generic disclosure did not render later selected species obvious under 35 U.S.C. § 103).

As described above, present claim 5 is directed to, *inter alia*, methods for screening a substance efficacious for healing, preventing or treating vascular disorders resulting from abnormal uric acid uptake or elimination by URAT1 comprising, *inter alia*, contacting a vascular smooth muscle cell with a test compound and urate. In contrast, claims 1-3 of the '847 patent are not directed to this subject matter. Nothing in the '847 patent claims even suggests a screening method using a vascular smooth muscle cell. In the absence of an express or inherent disclosure of a screening method using a vascular smooth muscle cell, the instant claims simply cannot be anticipated. Likewise, there is no disclosure in the prior claims that provides a reason to associate URAT1 with vascular smooth muscle cells. Accordingly, as claims 1-3 of the '847 patent do not teach every element set forth in claim 5 of the present application, claims 1-3 of the '847 patent do not anticipate or render obvious claim 5 of the present application.

For at least the above reasons, it is respectfully submitted that the present invention is patentably distinct from claims 1-3 of the '847 patent.

Reconsideration and withdrawal of the rejection are requested.